REMARKS

Status of the Claims

Claims 64, 65, 68-70, 72, 74, 75, 91-103, 132, 145, 147-148 and 150-174 are pending.

Claims 64, 65, 68-70, 72, 74, 75, 91-103, 132, 145, 147, 148 and 150-174 have been rejected.

Upon entry of this amendment, claims 64, 65, 68-70, 72, 74, 75, 91-103, 132, 145, 147, 148 and 150-174 will be pending.

Summary of the Amendment

Claim 169 and 174 have been amended to correct typographical errors.

Claim 170 has been amended that the antibody is administered for at least 6 hours. Support for the amendment can be found throughout the specification and claims as-filed.

No new matter has been added.

Objections

Claims 169 stand objected due to a typographical error. The typographical error has been corrected, rendering this objection moot.

Claim 174 stands objected to for being allegedly being in improper form. Applicants have amended claim 174 so that it no longer depends upon another multiple dependent claim. Therefore the objection is moot.

In view of the foregoing, Applicants respectfully request that the objection to the claims be withdrawn.

Rejection under 35 U.S.C. § 112, second paragraph

Claim 174 stands rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite. The Office alleges that there is insufficient antecedent basis for the phrase "the cytostatically effective amount" in reference to claim 171. Applicants have amended claim 174

to depend upon claim 169. There is sufficient antecedent support in view of the amendment. Accordingly, the claim is definite.

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 112, second paragraph be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 64, 65, 68-70, 72, 74, 75, 91-103, 132, 145, 147-148, and 150-174 stand rejected under 35 U.S.C. § 112, first paragraph for allegedly not being enabling for the full scope of the claim. The Office alleges that the while being enabling for an anti-guanylyl cyclase C antibody or a guanylyl cyclase C binding fragment thereof conjugated to a therapeutic agent, the present application is allegedly not enabled where the antibody or a guanylyl cyclase C binding fragment thereof is not conjugated to a therapeutic agent. The Office also alleges that the claims are not enabled for the recited doses and time periods for sustaining the doses. Applicants respectfully disagree.

The presently claimed invention is enabled because one of skill in the art would not need to be use undue experimentation to practice the claimed invention. The Office alleges that "other than uroguanylin, the art does not teach that unconjugated GCC ligands can treat primary or metastasized colorectal cancer and the development of therapeutics for malignant disorders such as colorectal cancer is well known in the art to be unpredictable." (Office Action, page 8). The Office cites Gura (Science, 1997, 278:1041-1042) as evidence of the unpredictability. The Office, however, has not provided any reasonable evidence to question the enablement of the presently claimed invention. there is nothing in the references cited by the Office that supports a reasonable basis to question the enablement of the presently claimed invention.

As the M.P.E.P. explains, "in order to make a rejection, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed

invention. (M.P.E.P. § 2164.04, citing *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)) "It is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." *In re Marzocchi* 439 F.2d at 224, 169 USPQ at 370 (CCPA 1971). The Examiner has not put forward any evidence other than evidence that certain compounds may not gain FDA marketing approval. This standard, however, is not the standard for patentability.

The presently claimed invention is directed to various methods. The cited references demonstrate the methods, such as those presently claims, are not unpredictable to the point where undue experimentation would be required. Whether the presently claimed methods are sufficient to gain FDA marketing approval is an unrelated and separate issue. The Office's citation of Young *et al.* (U.S. Patent Application No. 2004/0180002) does not support the Office's rejection. In contrast, Young supports that conclusion that the presently claimed invention is enabled. Young describes an antibody that can halt tumor progression. Young also refers to clinical trial data where success in at least one patient was also shown. These results do not show that the methods are not enabled, but rather that one of skill in the art would understand that nothing more than following the specification and, at most, routine experimentation would be required to practice the presently claimed methods. Predictability of FDA approval for marketing a therapeutic is not required to satisfy the enablement requirement.

The Office also alleges that it would not have been predicable to maintain a concentration as recited in the claims. The Office provides no evidence other than generalized conclusions that the ligands "may be degraded *in vivo* before achieving the claimed concentrations." The Office also states that "it ***appears*** that undue experimentation would be required to practice the claimed invention." (emphasis added, Office Action, page 10). The standard used by the Office is not sufficient to shift the burden. A claim cannot just "appear" to require undue experimentation, rather a claim is not enabled if undue experimentation would be required. Thus, the Office's

standard in concluding that the claims are not enabled is incorrect. The Office also fails to support the enablement rejection with any evidence. As discussed above, the Office must establish that there is a reasonable basis to question the enablement. Here, the Office has not established a reasonable basis because the allegations are unsubstantiated. If the rejection is maintained Applicants respectfully request that the Office submit an affidavit attesting to the facts used to conclude that the claims are not enabled.

In contrast to the Office's rejection, the specification provides how to administer the ligand and at what concentrations. One of skill in the art can follow the specification without having to perform undue experimentation. None of the references cited by the Office contradict the present specification and none of the references establish a reasonable basis to question the enablement of the present claimed invention. Accordingly, the claims are enabled.

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph alleging that the claims are not enabled be withdrawn.

Claims 64, 65, 68-70, 72, 74, 75, 91-103, 132, 145, 147-148, 150-169, 171, 172, and 174 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. The Office alleges that phrases

> wherein the cytostatically effective amount of an unconjugated guanylyl cyclase C ligand/antibody is an amount sufficient to maintain a concentration ≥EC50 of said unconjugated guanylyl cyclase C ligand for at least 15 or at least 30 days; or
>
> wherein the cytostatically effective amount of a guanylyl cyclase C ligand is an amount sufficient to maintain a plasma concentration ≥EC50 of said guanylyl cyclase C ligand in claims 64, 65, 68-70, 72, 74, 75, 91-103, 132, 145, 147-148, 150-169, 171, 172 and 174

constitutes new matter. (Office Action, page 11). Applicants respectfully disagree.

The phrases are supported by the as-filed application because one of skill in the art would immediately be able to envisage the claimed invention. As previously discussed, the specification provides support for the times lengths of 15 and 30 days. The specification must be read as a whole. The Office cannot take each instance where a certain dosage or concentration is referred to read it in isolation. One of skill in the art reading the specification would read it as a whole and would be able to immediately envisage the presently claimed invention. The Office's interpretation of the specification is too restrictive and, therefore, improper.

For example, at ¶ 127, the specification states that the ligand can be "administered into the circulatory system." Additionally, the specification states at ¶ 128 that the ligand can be administered at a "sufficient level" to "maintain the concentration of the ligand." to achieve a the desired effect. The specification also discusses various doses, concentrations, and time durations with respect to the level that is maintained to achieve the desired effect. For example, at ¶ 177 the specification describes an administration of a dose that is sufficient for the concentration of the ligand to "stay at or above the EC_{50}." The specification describes maintaining the effective amount for various amounts of times, such as 20 hours. For example, at ¶ 128 the specification states that the ligand "must be present at a sufficient level for a sustained amount of time" to achieve the desired effect on the cells. Claims 64, 65, and 167-169 recite that a concentration is maintained for at least 15 days and/or 30 days. Support for these claims can be found where the specification describes various "Dosage Regimens" at ¶ 169-171. Under the heading of "Dosage regimens" the specification describes regimens that lasts for at least 15 and 30 days. Claim 166 states that the ligand is infused into the individual for at least 6 hours. Support for this claim can be found, for example, in the as-filed claims. Claims 171 and 172 recite methods that comprises the sequential administration, as opposed to simultaneous administration, of the ligand and a different therapeutic agent. That is, the ligand is administered prior to the administration of a different therapeutic agent. Support for these claims can be found, for example, at ¶ 18 where the specification describes that the methods of the claims can be "followed by" another step of administering a different therapeutic agent. With respect to new claim 176, the specification also

states that the concentration can be maintained at an amount that is greater than or equal to ten times the EC_{50}. (Specification, ¶ 180 and 190). One of skill in the art would be able to immediately envisage the pending claims, thereby satisfying the written description requirement.

Applicants will also enclose under separate cover a declaration stating that one of skill in the art would be able to immediately envisage the dosages and concentrations recited in the pending claims from the as-filed specification.

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph alleging that the claims contain new matter be withdrawn.

Rejection under 35 U.S.C. § 102

Claims 170-172 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by U.S. Patent No. 5,879,656. The Office alleges that the claims have a reasonable interpretation to include antibodies conjugated to a therapeutic agent. Applicants have amended claim 170, solely in order to further prosecution, to recite that the antibody is administered for at least 6 hours. Accordingly, the '656 patent fails to anticipate the claims.

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 102(b) be withdrawn.

Claims 170-173 stand rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent No. 6,767,704. The Office alleges that the claims have a reasonable interpretation to include antibodies conjugated to a therapeutic agent. Applicants will enclose under separate cover a declaration stating that the invention disclosed was not invented by another an is, therefore, not prior art under 35 U.S.C. § 102(e). Accordingly, the rejection will be obviated in view of the declaration.

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 102(e) be withdrawn.

Rejection under 35 U.S.C. § 103

Claim 173 stands rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 5,879,656 in view of Queen *et al.* (PNAS, 1989, Vol. 86, pp. 10029-10033) and in further view of Riechmann *et al* (Nature Vol. 332:323-327). Claim 173 depends from claim 170, which has been amended. The cited references alone or in combination do not yield the presently claimed invention. Accordingly, claim 173 is not obvious.

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 103 be withdrawn.

Double Patenting

Claims 170-173 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting gas being unpatentable over claims 30-32, 35-38, 40-55, and 57-65 of copending Application No. 10/866,951 in view of Cohen (Int J. Radiat Oncol Biol Phys, 1987, 13:251-8) in further view of Queen *et al.* (PNAS, 1989, Vol. 86, pp. 100029-100033) in further view of Riechmann *et al.* (Nature, Vol. 332: 323-327, 1988).

Claims 170-173 are provisionally rejected on the ground of nonstatutory obviousness type double patenting as being unpatentable over claims 1, 2, 5, 7, 9, 10, 15-18, 23, 28-35, 38-43, 46-50, and 53-58 of U.S. Patent No. 5,879,656 in view of Cohen (Int J. Radiat Oncol Biol Phys, 1987, 13:251-8) in further view of Queen *et al.* (PNAS, 1989, Vol. 86, pp. 100029-100033) in further view of Riechmann *et al.* (Nature, Vol. 332: 323-327, 1988).

Claims 170-173 are provisionally rejected on the ground of nonstatutory obviousness type double patenting as being unpatentable over claims 6-8 of U.S. Patent No. 6,060,037 in view of U.S. Patent No. 5,879,656, in view of in view of Cohen (Int J. Radiat Oncol Biol Phys,

1987, 13:251-8) in further view of Queen *et al.* (PNAS, 1989, Vol. 86, pp. 100029-100033) in further view of Riechmann *et al.* (Nature, Vol. 332: 323-327, 1988).

Claims 170-173 are provisionally rejected on the ground of nonstatutory obviousness type double patenting as being unpatentable over claims 14-16 of U.S. Patent No. 6,087,109 in view of U.S. Patent No. 5,879,656, in view of in view of Cohen (Int J. Radiat Oncol Biol Phys, 1987, 13:251-8) in further view of Queen *et al.* (PNAS, 1989, Vol. 86, pp. 100029-100033) in further view of Riechmann *et al.* (Nature, Vol. 332: 323-327, 1988).

In view of the amendment to claim 170, which recites that the antibody is administered for at least 6 hours the obviousness-type double patenting rejections have been obviated. Accordingly, the presently claimed invention is not obvious and, thus, not subject to an obviousness-type double patenting rejection.

In view of the foregoing, Applicants respectfully request that the obviousness-type double patenting rejections be withdrawn.

Conclusion

Claims 64, 65, 68-70, 72, 74, 75, 91-103, 132, 145, 147, 148 and 150-174 are in condition for allowance. A notice of allowance is earnestly solicited.

The Commissioner is hereby authorized to charge any deficiencies of fees and credit of any overpayments to Deposit Account No. 50-0436.

Respectfully submitted,

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